PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Val Sheffield et al.

Serial No.: 10/025,187

Filed: December 18, 2001

For: A BARDET-BIEDL SUSCEPTIBILITY GENE AND USES THEREOF

Group Art Unit: 1645

Examiner: Roy R. Teller

Atty. Dkt. No.: IOWA:034US/SLH

BRIEF ON APPEAL

CERTIFICATE OF MAILING
37 C.F.R §1.8

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Steven L. Highlander

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Sir:

This Brief on Appeal is filed in response to Office Action mailed on January 11, 2005, regarding the above-captioned application. The deadline for this brief is June 13, 2005, by virtue of the Notice of Appeal received on April 13, 2005. The fee for this brief is included herewith; if the fee is missing or deficient, appellants authorize the Commissioner to debit Fulbright & Jaworski L.L.P. Deposit Account No. 55-1212/IOWA:034US/SLH.

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I. Real Party in Interest

The real party in interest of this application is the assignee, the University of Iowa Research Foundation, Iowa City, IA, and the licensee, Correlagen, Inc., Cambridge, MA.

II. Related Appeals and Interferences

There are no know related appeals or interferences.

III. Status of Claims

Claims 42-53 are pending and on appeal. The claims are listed in Appendix A to this brief.

IV. Status of Amendments

No unentered amendments have been offered.

V. Summary of Invention

In one aspect, the present invention involves a method of diagnosing Bardet-Biedl Syndrome (BBS) by identifying a mutation in a NGVN polypeptide or nucleic acid. Specification at page 5, lines 14-15. The methods may involve identifying a mutation in a NGVN polypeptide, for example, using immunologic analysis with a NGVN-binding monoclonal antibody or polyclonal antiserum (*e.g.*, ELISA, RIA, or Western blot). *Id.* at lines 18-21. The method may identify a particular mutation selected from the group consisting of $Val_{75}\rightarrow Gly$, $Arg_{272}\rightarrow Stop$, $Arg_{275}\rightarrow Stop$, and $Ile_{123}\rightarrow Val$. *Id.* at lines 21-22.

Alternatively, the method may involve identifying a mutation in a NGVN nucleic acid,

either mRNA, genomic DNA or cDNA, such as by amplification of said nucleic acid, hybridization of a nucleic acid to a labeled nucleic acid probe, and/or sequencing of a NGVN nucleic acid. *Id.* at lines 22-26. The method may identify a mutation selected from the group consisting of $T_{224}\rightarrow G$, $C_{814}\rightarrow T$, $C_{823}\rightarrow T$, $A_{387}\rightarrow G$, $A_{1413}\rightarrow C$, A_{940}del and 1206insA. *Id.* at 26-28.

VI. Issues

Whether the claims are properly rejected under 35 U.S.C. §103 as obvious over Landegren *et al.* in view of Hoang *et al.*

VII. Grouping of Claims

Claims 46 and 53 provide separate grounds for patentability, as discussed below in the final paragraph of section VIII(B).

VIII. Argument

A. Standard of Review

As an initial matter, appellant notes that findings of fact and conclusions of law by the U.S. Patent and Trademark Office must be made in accordance with the Administrative Procedure Act, 5 U.S.C. § 706(A), (E), 1994, and *Dickinson v. Zurko*, 527 U.S. 150, 158 (1999). Moreover, the Federal Circuit has held that findings of fact by the Board of Patent Appeals and Interferences must be supported by "substantial evidence" within the record. *In re Gartside*, 203 F.3d 1305, 1315 (Fed. Cir. 2000). In *In re Gartside*, the Federal Circuit stated that "the 'substantial evidence' standard asks whether a reasonable fact finder could have arrived at the agency's decision." *Id.* at 1312. Accordingly, it necessarily follows that an Examiner's position

on Appeal must be supported by "substantial evidence" within the record in order to be upheld by the Board of Patent Appeals and Interferences.

B. Rejection Under 35 U.S.C. §103

Claims 42-53 are rejected under 35 U.S.C, §103 over Landegren *et al.* in view of Hoang *et al.* Landegren is cited as teaching methods of assaying nucleic acids for possible mutation at a target nucleotide position, particularly in the context of diagnosing infectious or genetic disease. Hoang is cited as teaching chromosomal mapping of the KIFC3 gene within the BBS2 locus and that the expression pattern correlates well with clinical symptoms of BBS. The examiner thus posits that it would have been obvious to combine the technique of Landegren with the "beneficial teachings of Hoang," thereby rendering the present claims obvious. Appellants traverse.

In order for a valid *prima facie* case to stand under 35 U.S.C. §103, three basic criteria must be met: (1) the prior art reference (or references when combined) must teach or suggest all the claim limitations; (2) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (3) there must be a reasonable expectation of success. *Manual of Patent Examining Procedure* § 2142. See also *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed Cir. 1991) (emphasizing that the teaching or suggestion to make the claimed combination and the reasonable expectation of success must be both found in the prior art, and not based on applicant's disclosure). It is the first element of the preceding test that fails the rejection here.

There is no question that Landegren provides relevant teachings regarding methods of genetic diagnosis. However, Landegren teaches nothing with respect to (a) BBS or (b) NGVN.

Thus, these elements of the claimed invention must come from Hoang. However, while a review of that reference reveals a discussion of BBS, it clearly provides no mention of NGVN. Rather, Hoang describes the KIFC3 gene, a retinal kinesin gene, having the following amino acid sequence:

MVENERLRQEMRRCEAELQELRTKPAGPCPGCEHSQESAQLRDKLSQLQLEMAESKGM
LSELNLEVQQKTDRLAEVELRLKDCLAEKAQEEERLSRRLRDSHETIASLRAQSPPVK
YVIKTVEVESSKTKQALSESQARNQHLQEQVAMQRQVLKEMEQQLQSSHQLTARLRAQ
IAMYESELERAHGQMLEEMQSLEEDKNRAIEEAFARAQVEMKAVHENLAGVRTNLLTL
QPALRTLTNDYNGLKRQVRGFPLLLQEALRSVKAEIGQAIEEVNSNNQELLRKYRREL
QLRKKCHNELVRLKGNIRVIARVRPVTKEDGEGPEATNAVTFDADDDSIIHLLHKGKP
VSFELDKVFSPQASQQDVFQEVQALVTSCIDGFNVCIFAYGQTGAGKTYTMEGTAENP
GINQRALQLLFSEVQEKASDWEYTITVSAAEIYNEVLRDLLGKEPQEKLEIRLCPDGS
GQLYVPGLTEFQVQSVDDINKVFEFGHTNRTTEFTNLNEHSSRSHALLIVTVRGVDCS
TGLRTTGKLNLVDLAGSERVGKSGAEGSRLREAQHINKSLSALGDVIAALRSRQGHVP
FRNSKLTYLLQDSLSGDSKTLMVVQVSPVEKNTSETLYSLKFAERVRSVELGPGLRRA
ELGSWSSQEHLEWEPACQTPQPSARAHSAPSSGTSSRPGSIRRKLQPSGKSRPLPV

Hoang, FIGURE 1. Indeed, Hoang indicates that this gene has potential relevance to BBS, as lying within the BBS2 locus, thereby implicating its value in diagnosis of the BBS disease state. Nonetheless, the relevance of this observation, and the Hoang paper as a whole for that matter, is completely unclear. The present invention provides for diagnosis of BBS by detecting mutations in ***a NGVN polypeptide – a completely different protein than that encoded by the KIFC3 gene.*** The difference is plain to see by reference to the sequence of this protein:

MLLPVFTLKLRHKISPRMVAIGRYDGTHPCLAAATQTGKVFIHNPHTRNQHVSASRVF
QSPLESDVSLLSINQAVSCLTAGVLNPELGYDALLVGTQTNLLAYDVYNNSDLFYREV
ADGANAIVLGTLGDISSPLAIIGGNCALQGFNHEGSDLFWTVTGDNVNSLALCDFDGD
GKKELLVGSEDFDIRVFKEDEIVAEMTETEIVTSLCPMYGSRFGYALSNGTVGVYDKT
SRYWRIKSKNHAMSIHAFDLNSDGVNELITGWSNGKVDARSDRTGEVIFKDNFSSAIA
GVVEGDYRMDGHIQLICCSVDGEIRGYLPGTAEMRGNLMDTSAEQDLIRELSQKKQNL
LLELRNYEENAKAELASPLNEADGHRGIIPANTRLHTTLSVSLGNETQTAHTELRIST
SNDTIIRAVLIFAEGIFTGESHVVHPSIHNLSSSICIPIVPPKDVPVDLHLKAFVGYR
SSTQFHVFESTRQLPRFSMYALTSLDPASEPISYVNFTIAERAQRVVVWLGQNFLLPE
DTHIQNAPFQVCFTSLRNGGHLHIKIKLSGEITINTDDIDLAGDIIQSMASFFAIEDL
QVEADFPVYFEELRKVLVKVDEYHSVHQKLSADMADHSNLIRSLLVGAEDARLMRDMK
TMKSRYMELYDLNRDLLNGYKIRCNNHTELLGNLKAVNQAIQRAGRLRVGKPKNQVIT
ACRDAIRSNNINTLFKIMRVGTASS

SEQ ID NO:2. That NGVN is distinct from KIFC3 is clear from the sequences, which are nothing alike. Thus, there is no reference of record that mentions a NGVN protein or nucleic acid, much less one that would provide a link between NGVN and the BBS2 locus or BBS generally. As a matter of law, therefore, the rejection clearly is improper in failing to teach each limitation of the claimed invention.

Moreover, claims 46 and 53 provide listings of specific mutations in the NGVN polypeptide and coding region, respectively. The cited art is completely silent on such changes (not surprisingly, since it fails to even address the NGVN polypeptide or gene!!), and the examiner has not even attempted to argue that such specific changes would be obvious in view of the teachings provided in the cited art. As such, these claims provide separate grounds for patentability, above and beyond those discussed above for the remaining claims directed to the NVGN generally.

IX. Conclusion

In light of the foregoing, appellants respectfully submit that all claims are non-obvious and therefore, reversal of the rejection is respectfully requested.

Respectfully submitted,

June 13, 2005
Date

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APPENDIX A – COPY OF PENDING CLAIMS

1-41. (Canceled)

42. (Original) A method of diagnosing Bardet-Biedl Syndrome (BBS) comprising identifying a mutation in a NGVN polypeptide or nucleic acid.

43. (Original) The method of claim 42, wherein said method comprises identifying a mutation in a NGVN polypeptide.

44. (Original) The method of claim 43, wherein said method comprises immunologic analysis using a NGVN-binding monoclonal antibody or polyclonal antiserum.

45. (Original) The method of claim 44, wherein said immunologic analysis comprises ELISA, RIA, or Western blot.

46. (Original) The method of claim 43, wherein said method comprises identifying a mutation selected from the group consisting of $Val_{75}\rightarrow$Gly, $Arg_{272}\rightarrow$Stop, $Arg_{275}\rightarrow$Stop, and $Ile_{123}\rightarrow$Val.

47. (Original) The method of claim 42, wherein said method comprises identifying a mutation in a NGVN nucleic acid.

48. (Original) The method of claim 47, wherein said nucleic acid is a NGVN mRNA.

49. (Original) The method of claim 47, wherein said nucleic acid is a NGVN genomic DNA.

50. (Original) The method of claim 47, wherein said method comprises amplification of said nucleic acid.

51. (Original) The method of claim 47, wherein said method comprises hybridization of said nucleic acid to a labeled nucleic acid probe.

52. (Original) The method of claim 47, wherein said method comprises sequencing of a NGVN nucleic acid.

53. (Original) The method of claim 47, wherein said method comprises identifying a mutation selected from the group consisting of $T_{224}\rightarrow G$, $C_{814}\rightarrow T$, $C_{823}\rightarrow T$, $A_{387}\rightarrow G$, $A_{1413}\rightarrow C$, A_{940}del and 1206insA.

54-67. (Canceled)

PTO/SB/21 (09-04) MODIFIED

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JUN 15 2005	**Application Number:**	10/025,187
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	First Named Inventor:	Val Sheffield
	Art Unit:	1645
	Examiner Name:	Roy R. Teller
Total Number of Pages in this Submission : _____	**Attorney Docket Number:**	IOWA:034US

ENCLOSURES *(check all that apply)*

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☐ Amendment/Reply
  - ☐ After Final
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